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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/557,796	04/25/2000	James Hoch	252/123	8950

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EXAMINER
LACOURCIERE, KAREN A

ART UNIT	PAPER NUMBER
1635	14

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/557,796	Applicant(s) HOCH ET AL.	
	Examiner Karen Lacourciere	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *99-129* is/are pending in the application.

4a) Of the above claim(s) *99-121* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *122-129* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

FILE COPY

DETAILED ACTION

The numbering of claims is not accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 95-125, submitted with the response filed Dec 3, 2001, have been renumbered as claims 99-129.

The Examiner would like to thank Applicant's representative, Melanie Webster, for providing a copy of the claims to issue in the parent case, 09/172,952.

Priority

Applicant amendments filed Dec 3, 2001 have complied with the conditions for receiving the benefit of the filing date of parent Application 09/172,952 under 35 U.S.C. 120.

Election/Restriction

Newly submitted claims 99-121 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

As originally presented, the claimed subject matter was drawn to a recombinant cell wherein the cell expresses one or more genes which express one or more proteins that provide a detectable signal in the presence of a compound and methods of detecting the compound using said cells. Newly submitted claims 99-121 are drawn to cells which comprise a nucleic acid which converts a source compound and a gene which converts a target compound and methods of detecting a source compound using said cells. These are materially different compositions and methods than the originally presented methods, since in the original claims the products of the nucleic acid comprised in the cells actively converted the compound being detected, whereas in the new claims, the nucleic acid and genes actively convert the source compound to be detected.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 99-121 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Response to Amendment

In response to the rejection of record, Applicant has canceled all pending claims, and submitted new claims, therefore, all rejections of record have been withdrawn. New grounds of rejection are set forth below.

New Grounds of Rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 128 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 128 recites a promoter "derived from" SEQ ID NO:19. One skilled in the art would not known the metes and bounds of the promoters used in the claimed method because it is unclear what changes and what degree of changes can occur in the sequence of a promoter to be considered to be "derived from" SEQ ID NO:19.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 122-126, 128 and 129 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 122-126, 128 and 129 are drawn to nucleic acids comprising a yiaJ responsive promoter transcriptionally linked to a reporter gene, cells comprising said promoter, and methods of detecting the presence absence or amount of ascorbate using cells comprising said nucleic acid.

The specification discloses one species of a nucleic acid encoding a yiaJ promoter, SEQ ID NO: 19. SEQ ID NO:19 corresponds to the genomic DNA encoding the full klebsiella oxytoca yia operon. SEQ ID NO:19 meets the written description requirement, however, claims 122-126, 128 and 129 are directed to encompass nucleic acids comprising corresponding promoter sequences from other species and methods which utilize these promoters. None of these sequences meet the written description provision of 35 USC 112, first paragraph. Claims 122-126, 128 and 129 are drawn to a broad genus of sequences (yiaJ promoters), but the specification discloses only one species of this genus. These species would not be representative of the claimed genus, such that one skilled in the art would recognize that the Applicant was in possession of the claimed genus. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 1, 19 and the E. coli yiaJ, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins utilized in the claimed methods, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only SEQ ID NO:19, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Response to Arguments

Applicant's arguments filed December 3, 2001 have been fully considered but they are not persuasive.

In response to the rejection of record of claims 75-79, 82-85, and 88-92 under 35 USC 112, first paragraph, for lack of writen description. These arguments have been considered to the extent that they read on the rejection on the basis of lack of written description set forth herein for claims 122-126, 128 and 129.

Applicant argues that the specification discloses the sequence of a yiaJ binding promoter within the 5' region of SEQ ID NO:19 and further discloses a schematic of the yiaK-S operon which depicts the location of the yiaJ promoter (fig 13, labeled P_{yia}) and discloses the general characteristics of a promoter. Applicant argues that in example 1, the yiaJ promoter region of SEQ ID NO:19 was replaced by the trp-lac hybrid promoter. Applicant argues that the art discloses the sequence of the full yia operon of E. coli and H. influenza and would be able to determine the sequence of the E. coli and H. influenza yiaJ promoters form the guidance in the specification. Applicant argues that given the guidance in the specification as to the full sequence of SEQ ID NO:19, the schematic representation of the location of the yiaJ promoter, the general description of promoter elements and the art disclosed sequence of the E. coli and H. influenza yia operons, one skilled in the art would recognize that applicants were in possession of the full genus of yiaJ promoter sequences at the time of the invention.

These arguments have not been found to be persuasive. Applicants have disclosed a full operon which comprises a yiaJ promoter and a drawing which indicates the position of the promoter relative to other sequences in the operon. Applicant has not described what sequence within the large operon is actually required for the promoter activity or what sequence elements within the klebsiella oxytoca yiaJ promoter would be common to other yiaJ promoters from other species. Applicant has provided a general description of elements common to promoters (see page 14, line 24-page 15, line 13), however, applicant has not provided a description of the structural characteristics (for example, sequence) specific to yiaJ promoters that would distinguish a yiaJ promoter from generally any other promoter. Applicants arguments related to the trp-lac promoter do not appear to be relevant to the written description of yiaJ promoters. Although the art discloses the full sequence of the yia operon for E. coli and H. influenza, neither the prior art, not the instant specification, discloses what sequence within these operons constitutes a yiaJ promoter and what elements of thes promoters would be common to all yiaJ promoters. Further, the disclosure of three species of yaiJ promoters would not be adequate to demonstrate to one skilled in the art that the inventor was in possession of the full genus of yiaJ promoters at the time of the instant invention, for example, yiaJ promoters from other species, including non-bacterial yiaJ promoters.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 122, 123 and 129 are rejected under 35 U.S.C. 102(a) as being anticipated by Badía et al.(reference AK on PTO form 1449, filed 04-25-00).

Badía et al. disclose an E. coli cell (for example, ECL1 strain) which comprises the E. coli yiaJ promoter transcriptionally linked to a reporter gene, L-xylose kinase, which produces the detectable signal of growth on L-lyxose. ECL1 expresses YiaJ, which results in the repression of expression of L-lyxose kinase. Badía discloses ECL1 as a recombinant cell, for example, see the "Material and Methods" section,first paragraph, which describes the recombinant phenotype of ECL1 relative to K12. Badía also disclose an isolated nucleic acid comprising the E. coli yiaJ promoter, transcriptionally linked to a reporter gene, L-xylose kinase, see, for example, page 8379, first column, first full paragraph, which discloses an isolated nucleic acid comprising the full E. coli yia operon. Therefore, Badía et al. anticipates claims 122, 123 and 129.

Response to Arguments

Applicant's arguments filed Dec 3, 2001 have been fully considered but they are not persuasive.

In response to the rejection of record, Applicant argues that Badía et al. do not disclose a yiaJ gene transcriptionaly linked to a CAT reporter, but instead disclose the CAT gene for insertional mutagenesis of yiaJ.

These arguments do not appear relevant to the rejection under 35 USC 102(a) set forth herein for newly submitted claims 122, 123 and 129, which now recite a nucleic acid and cells which comprise a yiaJ responsive promoter which is transcriptionally linked to a reporter gene.

Conclusion

Any rejection of record nto repeated herein is considered to be withdrawn.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (703) 308-7523. The examiner can normally be reached Monday-Thursday 8:30 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached at (703) 308-0447. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

ANDREW WANG
PRIMARY EXAMINER

Karen A. Lacourciere

February 11, 2002